PRECIS

According to statistics of the American Cancer Society, an estimated 55,000 individuals will be diagnosed with melanoma cancer and 8,000 will die of the disease this year in the United States despite all current therapy. This protocol attempts to exploit an approach to melanoma gene therapy using a naturally occurring barrier to xenotransplantation in humans in attempt to vaccinate patients against their melanoma. The expression of the murine α(1,3)galactosyltransferase [α(1,3)GT] gene results in the cell surface expression of α(1,3)galactosyl-epitopes (αgal) on membrane glycoproteins and glycolipids. These epitopes are the major target of the hyperacute rejection response that occurs when organs are transplanted from non-primate donor species into man. Human hosts often have pre-existing anti- α-gal antibodies that bind α-gal epitopes and lead to rapid activation of complement and cell lysis. The pre-existing anti-α-gal antibodies found in most individuals are thought to be due to exposure to α-gal epitopes that are naturally expressed on normal gut flora leading to chronic immunological stimulation. These antibodies may comprise up to 1% of serum IgG. In this Phase I/II trial, patients with recurrent or refractory advanced stage melanoma will undergo a series of four intradermal injections with a trivalent vaccine of composed of irradiated allogeneic melanoma cell lines (HAM-1, HAM-2 and HAM-3). These cell lines have been transduced with a recombinant Moloney murine leukemia virus (MoMLV)-based retroviral vector expressing the murine α(1,3)GT gene. Endpoints of the study include determination of dose-limiting toxicity (DLT), maximum tolerated dose (MTD), tumor and immunological responses.